

L6 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:654747 CAPLUS
DOCUMENT NUMBER: 135:222364
TITLE: DNA sequence of human prostaglandin E2 receptor 1 (
EP1-R) gene, and methods for the
diagnosis of **polymorphisms** thereof
INVENTOR(S): Smith, John Craig; Anand, Rakesh; Morten, John Edward
Norris
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1130122	A2	20010905	EP 2001-301291	20010213
EP 1130122	A3	20011017		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002076702	A1	20020620	US 2001-781311	20010213
JP 2001286288	A2	20011016	JP 2001-40076	20010216
PRIORITY APPLN. INFO.:			GB 2000-3553	A 20000217
			GB 2000-8376	A 20000406

AB The invention provides the genomic DNA sequence of the human
prostaglandin
E2 receptor 1 (EP1-R) gene; it differs from the cDNA sequence of EMBL
L22647 and the DNA sequence of EMBL AC008569. The invention also
provides
methods of diagnosing fourteen specific **polymorphisms** in the
EP1-R gene and novel allelic polypeptides encoded
thereby. The invention provides allele-specific probes and/or primers
for
use in diagnosis. The invention also relates to methods of diagnosis and
treatment of EP1-R ligand mediated diseases, such as cancer or arthritis.

L10 ANSWER 16 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000005672 MEDLINE
DOCUMENT NUMBER: 20005672 PubMed ID: 10537280
TITLE: Role of the **prostaglandin E receptor**
subtype **EP1** in colon carcinogenesis.
AUTHOR: Watanabe K; Kawamori T; Nakatsugi S; Ohta T; Ohuchida S;
Yamamoto H; Maruyama T; Kondo K; Ushikubi F; Narumiya S;
Sugimura T; Wakabayashi K
CORPORATE SOURCE: Cancer Prevention Division, National Cancer Center
Research Institute, Tokyo, Japan.
SOURCE: CANCER RESEARCH, (1999 Oct 15) 59 (20) 5093-6.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991110
AB Although the cyclooxygenase pathway of the arachidonic acid cascade has been suggested to play an important role in colon carcinogenesis, the molecular species of prostanoids and receptors involved have not been fully elucidated yet. We examined the development of aberrant crypt foci (ACFs), putative preneoplastic lesions of the colon, in two lines of knockout mice, each deficient in **prostaglandin E receptors**, EP1 and EP3, by treatment with the colon carcinogen, azoxymethane. Formation of ACFs was decreased only in the EP1-knockout mice to approximately 60% of the level in wild-type mice. Administration of 250, 500, or 1000 ppm of a novel selective EP1 antagonist, ONO-8711, in the diet to azoxymethane-treated C57BL/6J mice also resulted in a dose-dependent reduction of ACF formation. Moreover, when Min mice, having a nonsense mutation in the adenomatous polyposis coli gene, were given 500 ppm ONO-8711 in the diet, the number of intestinal polyps was significantly reduced to 57% of that in the basal diet group. These results strongly suggest that prostaglandin E2 contributes to colon carcinogenesis to some extent through its action at the EP1 receptor. Thus, EP1 antagonists may be good candidates as chemopreventive agents for colon **cancer**.

OF 19 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002179026 MEDLINE
DOCUMENT NUMBER: 21908116 PubMed ID: 11911260
TITLE: Evaluation of a selective prostaglandin E receptor EP1 antagonist for potential properties in colon carcinogenesis.
AUTHOR: Kawamori T; Uchiya N; Kitamura T; Ohuchida S; Yamamoto H; Maruyama T; Sugimura T; Wakabayashi K
CORPORATE SOURCE: Cancer Prevention Division, National Cancer Center Research Institute, Tokyo, Japan.. tkawamor@gan2.ncc.go.jp
SOURCE: ANTICANCER RESEARCH, (2001 Nov-Dec) 21 (6A) 3865-9.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020326
Last Updated on STN: 20020420
Entered Medline: 20020419
AB BACKGROUND: Cyclooxygenases (COXs) and prostanoids play pivotal roles in colon carcinogenesis. This study was designed to determine the chemopreventive effects of ONO-8711, a selective prostaglandin E receptor EP1 antagonist, on the development of azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) in male F344 rats and to compare its potential with that of nimesulide, a well-documented selective COX-2 inhibitor.
MATERIALS AND METHODS: Five-week-old male F344 rats received s.c. injections of AOM (15 mg/kg body weight) or the saline vehicle once weekly for two weeks and were fed the control diet (AIN-76A) or the experimental diets containing 400 or 800 ppm of ONO-8711 or 400 ppm nimesulide for 5 weeks. RESULTS: Administration of ONO-8711 at 800 ppm significantly reduced the total number of ACF/colon and 5-bromodeoxyuridine (BrdUrd) labeling index as compared to the control diet group (by 31% and 66%, respectively). As expected, dietary administration of nimesulide also suppressed the development of ACF and BrdUrd labeling index in the colon, by about 39% and 54%, respectively. CONCLUSION: Our finding that ONO-8711 significantly suppresses colonic ACF formation and cell proliferation strengthens the hypothesis that the selective **prostaglandin E receptor EP1** antagonists possesses chemopreventive activity against colon cancer development.

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5686498 9/99

RESULT 1
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DEFINITION Homo sapiens chromosome 19 clone CTC-548K16, complete sequence.
ACCESSION AC008569
VERSION AC008569.7 GI:15431055
KEYWORDS HTG.
SOURCE human.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.
TITLE Direct Submission
JOURNAL Unpublished
REFERENCE 2 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute.
TITLE Direct Submission
JOURNAL Submitted (03-AUG-1999) Production Sequencing Facility, DOE Joint
Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA
REFERENCE 3 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.
TITLE Direct Submission
JOURNAL Submitted (08-NOV-2000) DOE Joint Genome Institute, 2800 Mitchell
Drive, Walnut Creek, CA 94598, USA
REFERENCE 4 (bases 1 to 227245)
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.
TITLE Direct Submission
JOURNAL Submitted (05-SEP-2001) DOE Joint Genome Institute, 2800 Mitchell
Drive, Walnut Creek, CA 94598, USA
COMMENT On Sep 5, 2001 this sequence version replaced gi:11120757.
Draft Sequence Produced by DOE Joint Genome Institute
www.jgi.doe.gov
Finishing Completed at Stanford Human Genome Center
www-shgc.stanford.edu
Quality: Phrap Quality >=40 99.8% of Sequence;
Estimated Total Number of Errors is 0.3.
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SHGC-35463 G29823
SHGC-31833 G29335.
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Matches 3906; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

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RESULT 4
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 VERSION L22647.1 GI:410208
 KEYWORDS prostaglandin receptor epl subtype.
 SOURCE Homo sapiens cDNA to mRNA.
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 1376)
 AUTHORS Funk,C.D., Furci,L., FitzGerald,G.A., Grygorczyk,R., Rochette,C.,
 Bayne,M.A., Abramovitz,M., Adam,M. and Metters,K.M.
 TITLE Cloning and expression of a cDNA for the human prostaglandin E
 receptor EP1 subtype
 JOURNAL J. Biol. Chem. 268 (35), 26767-26772 (1993)
 MEDLINE 94075377
 REFERENCE 2 (bases 1 to 1376)
 AUTHORS Funk,C.D.
 TITLE Direct Submission
 JOURNAL Submitted (01-NOV-1993) Colin D. Funk, Department of Pharmacology,
 Vanderbilt University, Nashville, TN 37232, USA
 FEATURES Location/Qualifiers
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 ORIGIN

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 Qy 2291 ctgctgttcgtggccagccgtgtggccaccgcacccgtgtatcccggcg 2350
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 Db 294 CTGCTGTTCGTGGCCAGCCTGCTGGCCACCGACCTGGCGGGCACGTGATCCC GGCGCG 353

 Qy 2351 ctggtgctgcgtctgtacactgcggggcgcgctccggccggggcctgccacttctg 2410
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 Db 354 CTGGTGCTGCGTCTGTACACTGCGGGGCGCCTCCGGCCGGGGCCTGCCACTTCCTG 413

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 Db 414 GGCGGCTGCATGGTCTTCTTCGGCCTGTGCCCCGCTGCTGCTGGCTGTGGCATGGCGTG 473

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 Qy 2771 tggcgacgcgcgtcccgacggcctccccggctcaggccccacagccggcg 2830
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 Db 774 TGGCGACGCCGCTCCCGACGGCCTCCCCGGCCTCAGGCCCGACAGCCGGCGTCGCTGG 833

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 Db 894 ACCTTCTTGGCGGCTCTGGAGCAGCGGCTCGGCACGCAGAGCTCGCGCCACGACGTG 95

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Qy 3011 ctggtagggggcgcaccggccctcgagccacgctcctccgctccctctcgcc 3065
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RESULT 5
AR086516
LOCUS AR086516 1394 bp DNA linear PAT 07-SEP-2000
DEFINITION Sequence 3 from patent US 5985597.
ACCESSION AR086516
VERSION AR086516.1 GI:10013282
KEYWORDS .
SOURCE Unknown.
ORGANISM Unknown.
Unclassified.
REFERENCE 1 (bases 1 to 1394)
AUTHORS Ford-Hutchinson,A., Funk,C., Grygorczyk,R. and Metters,K.
TITLE DNA encoding prostaglandin receptor EP1
JOURNAL Patent: US 5985597-A 3 16-NOV-1999;
FEATURES Location/Qualifiers
source 1..1394
/organism="unknown"
BASE COUNT 157 a 525 c 484 g 228 t
ORIGIN

Qy 2411 ggcggctgcatggtcttcttcggcctgtgcccgtctgctgggctgtggcatggccgtg 2470
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Db 414 GGC GGCT GCATGGT CTTCTTCGGC CTGTGCCCGCTGCTGCTGGGCTGTGGCATGGCCGTG 473

Qy 2471 gagcgctgcgtggcgtaacgcggccgtctccacgcgcgcgggtctcggtcgccgc 2530
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Db 474 GAGCGCTGC GTGGCGTCACGC GGCGCTGCTCCACGCCGC CGCGGGTCTCGGT CGCCC GC 533

Qy 2531 gcgcgcctggcgctggccgcgtggcccggtggccctggccgtggcgctgtccgcgtg 2590
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Db 534 GCGCGCCTGGCGCTGGCCGCGGTGGCCCGGGTGGCCTTG GCCGTGGCGCTGCTGCCGCTG 593

Qy 2591 gcgcgcgtggccgcatacgactacccgggacgtggtgcttcatcgccctgggt 2650
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Db 1014 CTGGTGTGTTGGTGGCGCTGGCCGTCGGCGGCTGGAGCTACCTCCCTGCAGCGGC 1068

RESULT 6
AX280933
LOCUS AX280933 1209 bp DNA linear PAT 02-NOV-2001
DEFINITION Sequence 556 from Patent WO0177172.
ACCESSION AX280933
VERSION AX280933.1 GI:16608222
KEYWORDS .
SOURCE human.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (sites)
AUTHORS Lehmann-Bruinsma,K., Liaw,C.W. and Lin,I.L.
TITLE Non-endogenous, constitutively activated known g protein-coupled
receptors
JOURNAL Patent: WO 0177172-A 556 18-OCT-2001;
Arena Pharmaceuticals, Inc. (US)
FEATURES Location/Qualifiers
source 1. .1209
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BASE COUNT 107 a 469 c 424 g 209 t
ORIGIN

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|||
Db 541 CTGCAGTACCCGGGCACGTGGTGCCTCATCGGCCTGGTCCCCCGGGCGGCTGGCGCCAG 600

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Qy 2732 tgcaaacacgctcagggcctggccctgctacgcgcgcgtggcgcacgcgcgtcccacgg 2791
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Db 781 GCCTCCGCCTCGTCCGCCTCGTCCATCGCTCGCCTCCACCTCTTGGCGGCTCTCGG 840

Qy 2912 agcagcggtcgacgcacgcagagctcgccgcacgcacgtggagatggggccagcttgtc 2971
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Db 841 AGCAGCGGCTCGGCACGCAGAGCTCGCGCCACGACGTGGAGATGAAGGGCCAGCTTGTC 900

Qy 2972 ggtatcatgggtgtcgatctgtggagccaatgtgggtggggccgcaccggcc 3031
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Qy 3032 cctcgaggccacgcgtccctccgcgtccctctcgcc 3065
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Db 961 GTCGGCGGCTGGAGCTACCTCCCTGCAGCGGC 994